Int. J. Cancer: **77,** 549–553 (1998)

Publication of the International Union Against Cancer
Publication de l'Union Internationale Contre le Cancer

RISK FACTORS FOR COLORECTAL CANCER IN A PROSPECTIVE STUDY AMONG U.S. WHITE MEN

Ann W. Hsing[1]*, Joseph K. McLaughlin[2], Wong-Ho Chow[1], Leonard M. Schuman[3], Harvey T. Co Chien[4], Gloria Gridley[1], Erik Bjelke[5], Sholom Wacholder[1] and William J. Blot[2]

[1]*Divison of Cancer Epidmeiology and Genetics, National Cancer Institute, Bethesda, MD, USA*
[2]*International Epidemiology Institute, Rockville, MD, USA*
[3]*Division of Epidemiology, School of Public Health, University of Minnesota, Minneapolis, MN, USA*
[4]*Westat, Inc., Rockville, MD, USA*
[5]*Center for Epidemiologic Research, University of Bergen, Bergen, Norway*

The association of diet, smoking/drinking and occupation with subsequent risk of fatal colorectal cancer was investigated in a cohort of 17,633 white males aged 35 and older, who completed a mail questionnaire in 1966. During the subsequent 20 years of follow-up, 120 colon cancer and 25 rectal cancer deaths were identified. Due to small numbers, no significant dose-response trends were observed in the study, but risk of colon cancer was elevated among heavy cigarette smokers (≥30/day; RR = 2.3, 95% CI 0.9–5.7), heavy beer drinkers (≥14 times/month; RR = 1.9, 95% CI 1.0–3.8) and white-collar workers (RR = 1.7, 95% CI 1.0–3.0) or crafts workers within service and trade industries (RR = 2.6, 95% CI 1.1–5.8). In addition, an increased risk was seen for those who consumed red meat more than twice a day (RR = 1.8, 95% CI 0.8–4.4). Risk patterns for cancers of the colon and rectum combined were similar to those reported for cancer of the colon, but the estimates were somewhat dampened. Our findings support previous reports that a high intake of red meat and a sedentary life-style may increase the risk of colon cancer. ***Int. J. Cancer*** **77:549–553, 1998.**

Cancer of the colorectum is the second leading cause of cancer death in the United States (Parker *et al*., 1997); however, its etiology remains unclear (Schottenfeld and Winawer, 1996). Although familial adenomatous polyposis and a family history of colon cancer (hereditary non-polyposis colorectal cancer) predispose to colon cancer, only about 10% of the cancers are genetically related (Thomas, 1993). Results from international correlation and migrant studies suggest that environmental factors, especially dietary factors, are likely to account for most colon cancers (Armstrong and Doll, 1975).

Numerous case-control studies have suggested that a high intake of red meat, dietary fat (particularly from animal sources) and/or total energy and a low intake of fruits, vegetables and fiber increases the risk of colon cancer (Potter *et al*., 1994). Relatively few prospective studies have examined the role of diet in colon cancer risk, and the results are equivocal (Giovannucci *et al*., 1994*c*, 1997; Bostick *et al*., 1994; Steinmetz *et al*., 1994; Thun *et al*., 1992; Heilbrun *et al*., 1989; Willett *et al*., 1990). Two of these showed that intake of red meat and processed meat, but not total fat or total energy, was associated with an increased risk of colon cancer (Giovannucci *et al*., 1994*c*; Willet *et al*., 1990).

The role of smoking and alcohol use is also unclear. Although earlier studies have not found cigarette smoking to be related to excess risk of colon cancer (IARC 1986), several large prospective studies have shown that long-term cigarette smokers had increased risks of colon and rectal cancers (Giovannucci and Martinez, 1996; Giovannucci *et al*., 1994*a,b*; Heineman *et al*., 1994). Furthermore, consistent evidence has now emerged showing that the prevalence of pre-cancerous colon adenoma is increased among smokers (Giovannucci *et al*., 1994*b*; Martinez *et al*., 1995). Evidence for alcohol as a causal factor for cancer of the colon was considered inconclusive by IARC (1988). More recent data, however, suggest that intake of alcoholic beverages may be related to a weak but significant excess risk in colon cancer (Glynn *et al*. 1996; Kune and Vitetta, 1992; Longnecker *et al*., 1990).

Growing evidence indicates that a low level of physical activity, either occupational or non-occupational, increases the risk of colon cancer in men; the evidence is less convincing for women (Colditz *et al*., 1997). Although colon cancer is not considered an occupational cancer, excess risk of colon cancer has been reported for workers in the insulation industry, chemical plants, synthetic rubber manufacturing and oil refineries and for woodworkers in the automotive industry (Chow *et al*., 1994).

Based on data from a 20-year follow-up of 17,633 men in the Lutheran Brotherhood Study (LBS), we investigated further the associations of tobacco and alcohol use, diet and occupation with the risk of colorectal cancer mortality.

MATERIAL AND METHODS

The cohort

Methods of the study are described in detail elsewhere (Hsing *et al.,* 1990). Briefly, in 1966, 17,633 white male policyholders (68.5% of all policyholders) of the Lutheran Brotherhood Insurance Society completed a mail questionnaire. Respondents and non-respondents were comparable in age, urban/rural residence, policy status and cancer mortality at 11.5 years of follow-up (Snowden, 1981).

The mail questionnaire included information on demographic background, tobacco and alcohol use, diet, occupation and physical activity. The occupation and industry in which the respondents had worked for the longest period of time were elicited. Classification by major industry (mining/manufacturing, farming and other, *i.e.*, services, transportation, trade) and occupation (professional/clerical, crafts, laborer and farm worker) was used for analysis.

Respondents were asked about frequency of current (as of 1966) monthly consumption of 35 foods, which were grouped into 9 food groups for analysis. Of the 17,633 study subjects, 71% had no missing data on any food items 25% fewer than 5 missing items and 4% between 5 and 10 missing food items. Intake estimates for missing food items were imputed, using the median values of the remaining subjects stratified by urban/rural, education and age categories.

Mortality follow-up

Underlying and contributory causes of death and other significant conditions were obtained from death certificates and coded by a nosologist at the Minnesota State Department of Health. By 1986, after 20 years and 286,731 persons-years of follow-up, 4,513

*Correspondence to: National Cancer Institute, EPN 443, 6130 Executive Blvd., Bethesda, MD 20892, USA. Fax: (301) 496-1691. E-mail:hsinga@epndce.nci.nih.gov

Received 20 March 1998

deaths (26% of the cohort) had occurred. Another 4,027 subjects (23%) were lost to follow-up due to maturation or lapse of their policies. A separate study, which obtained death certificates for all deceased subjects in the LBS cohort regardless of policy status, showed that at 11.5 years of follow-up no significant differences in age, urban/rural residence, vital status or cause of death were detected between the active members and those who were lost to follow-up (Snowden, 1981).

Statistical analysis

Age-adjusted relative risks (RRs) of colon cancer mortality were calculated using a Poison regression program (AMFIT) for modeling hazard functions with grouped data (Breslow and Day, 1987; Preston *et al.*, 1985). Five-year age intervals were used for the grouping of data. RRs for colon cancer were calculated for each age stratum and summarized over all strata for the selected variables. Person-years were accumulated up to death, loss to follow-up or the end of the study in 1986. Urban/rural residential status was used as an adjustment variable because the pattern of smoking, alcohol use and diet is different between urban and rural residents. Rural subjects smoked and drank (both alcohol and beer) less; consumed more meat, milk and eggs; and exercised more.

Since 78% of the colon cancer deaths in the study had no specific subsite information coded on the death certificate, all colon cancer deaths were combined for the analysis. In addition, a separate analysis of colorectal cancer was conducted, since the number of rectal cancer deaths was small (n = 25) and the distinction between these 2 sites on death certificates is not good (there is a tendency to over-report colon cancer and to under-report rectal cancer deaths) (Chow and Devesa, 1992), though certain risk factors for cancers of the colon and rectum may be different. In all tables, 2 sets of risk estimates are presented, one for cancer of the colon and one for cancers of the colon and rectum combined.

RESULTS

A total of 120 colon cancer and 25 rectal cancer deaths had occurred by 1986. The median age at colorectal cancer death was 68. There were only small, non-significant differences in risk of colon cancer related to marital status, education or residence, though those who lived in urban areas had a 30% excess risk (95% CI 0.9–1.9).

Table I shows that tobacco use was associated with a 40–60% increased risk of colon cancer. Among current cigarette smokers, the risk of cancer death increased with the number of cigarettes smoked, with RRs ranging from 1.1 (95% CI 0.5–2.5) for smokers of less than 20 cigarettes per day to 2.3 (95% CI 0.9–5.7) for those who smoked more than 30 cigarettes per day. No consistent trend with duration or intensity of smoking was observed, however. RRs were dampened when cancers of the colon and rectum were combined for analysis.

For cancer of the colon, mild excesses in risk were found among ever drinkers of beer, hard liquor or total alcohol (Table II). Trends with amount of drinking were not smooth, but one of the highest RRs was found among heavy beer drinkers (≥14 drinks/month; RR = 1.9, 95% CI 1.0–3.8). Risk patterns were similar for colorectal cancer.

Table III shows that after adjustment for other risk factors, crafts workers (RR = 2.6, 95% CI 1.1–5.8) and white-collar workers within the service and trade industries (RR = 1.7, 95% CI 1.0–3.0) had significantly elevated risks for colon cancer. In addition, men who had moderate to heavy physical exercise (self-reported) had a slightly reduced risk (10–30%), but the trend was not smooth nor was it statistically significant (data not shown). Similar associations were observed when cancers of the colon and rectum were combined.

Risks of colon and colorectal cancer according to consumption of 9 food groups are shown in Table IV. An increased risk of colon cancer was associated with heavy consumption of red meat (≥2 times per day; RR = 1.8, 95% CI 0.8–4.4), though the trend was not significant. Increasing risks also were observed with frequency of consumption of fish, eggs and vegetables but with no significant linear trends. For fruits, an increased risk with frequency of consumption was noted and the linear trend was significant. A reduction in risk was related to consumption of dairy products (milk and ice cream). No clear risk patterns were seen for poultry, cruciferous vegetables or bread. Similar risk patterns were observed for colorectal cancer.

DISCUSSION

In this 20-year follow-up study, elevated risk of colorectal cancer mortality was found among cigarette smokers, heavy beer drinkers, white-collar workers and crafts workers within service and trade industries. Risk also was increased among those who consumed red meat twice or more per day, while a moderate protective effect was seen for dairy products but not for vegetables or fruits.

Similar to two previous prospective studies (Giovannuci *et al.*, 1994*a,b*; Willett *et al.*, 1990), our data indicate that a high intake of red meat was associated with an increased risk of colon cancer death, though the trend was not smooth. Meat and fat have been the major suspect risk factors for colon cancer due to the strong

TABLE I – RELATIVE RISK (RR) OF COLORECTAL CANCER MORTALITY ASSOCIATED WITH LEVEL OF TOBACCO USE, LUTHERAN BROTHERHOOD COHORT (1966–1986)

Tobacco use as of 1966[1]	Cohort (person-years)	Colon (n = 120)			Colon and rectum (n = 145)		
		Number of deaths	RR[2]	95% CI[3]	Number of deaths	RR[2]	95% CI[3]
Never used tobacco	58,888	16	1.0	—	26	1.0	—
Used tobacco other than cigarettes	27,025	16	1.6	0.8–3.2	17	1.0	0.5–1.9
Cigarette smokers							
Occasional[4]	28,915	12	1.4	0.7–2.9	15	1.1	0.6–2.0
Ex-smokers	78,827	38	1.5	0.8–2.7	44	1.1	0.7–1.8
Current smokers	82,896	29	1.4	0.7–2.7	32	1.0	0.6–1.7
1–19 cigarettes/day	29,404	9	1.1	0.5–2.5	10	0.8	0.4–1.6
20–29 cigarettes/day	36,589	13	1.6	0.7–3.4	14	1.1	0.5–2.1
≥30 cigarettes/day	15,732	7	2.3	0.9–5.7	8	1.7	0.7–3.8
		Linear trend $p = 0.25$			Linear trend $p = 0.49$		
Years of smoking							
1–19	11,533	1	1.3	0.2–9.7	1	0.8	0.1–6.0
20–29	34,460	11	2.4	1.0–5.3	11	1.5	0.7–3.2
≥30	35,548	17	1.2	0.6–2.4	20	0.9	0.5–1.6
		Linear trend $p = 0.79$			Linear trend $p = 0.77$		

[1]Subjects with missing information on tobacco use were excluded.–[2]Adjusted for age, urban/rural residence and alcohol intake.–[3]95% confidence interval.–[4]Occasional users generally smoked less than one cigarette, pipe or cigar per day.

TABLE II – RELATIVE RISK (RR) OF COLORECTAL CANCER MORTALITY BY CONSUMPTION OF ALCOHOLIC BEVERAGES, LUTHERAN BROTHERHOOD COHORT (1966–1986)

Number of drinks[1]	Cohort (person-years)	Colon (n = 120)			Colon and rectum (n = 145)		
		Number of deaths	RR[2]	95% CI[3]	Number of deaths	RR[2]	95% CI[3]
Total alcohol (times/month)							
Never	59,818	22	1.0	—	29	1.0	—
Ever	191,040	77	1.4	0.9–2.3	91	1.4	0.9–2.2
1–2	74,440	31	1.4	0.8–2.4	37	1.4	0.8–2.3
3–9	44,594	16	1.3	0.7–2.5	20	1.4	0.8–2.4
≥10	72,005	30	1.5	0.8–2.7	34	1.5	0.9–2.5
		Linear trend $p = 0.18$			Linear trend $p = 0.17$		
Beer (drinks/month)							
Ever	208,890	93	1.5	0.9–2.4	107	1.4	0.9–2.2
1–2	91,614	40	1.4	0.8–2.4	47	1.4	0.9–2.3
3–5	39,099	15	1.4	0.7–2.8	19	1.5	0.8–2.7
6–13	28,601	6	0.8	0.3–2.0	7	0.8	0.3–1.9
≥14	29,818	16	1.9	1.0–3.8	18	2.0	1.0–3.6
Used before[4]	19,763	16	2.1	1.1–4.0	16	1.7	0.9–3.3
		Linear trend $p = 0.19$			Linear trend $p = 0.17$		
Hard liquor (drinks/month)							
Ever	190,070	73	1.3	0.8–2.0	87	1.3	0.8–2.1
1–2	100,460	37	1.3	0.7–2.2	44	1.3	0.8–2.1
3–5	31,179	12	1.3	0.6–2.6	15	1.3	0.7–2.6
6–13	22,217	8	1.2	0.5–2.8	9	1.2	0.5–2.6
≥14	19,693	8	1.3	0.5–3.0	9	1.2	0.6–2.7
Used before[4]	16,522	8	1.3	0.6–2.9	10	1.3	0.6–2.8
		Linear trend $p = 0.65$			Linear trend $p = 0.64$		

[1]Subjects with missing information on alcohol intake were excluded.–[2]Adjusted for age, urban/rural residence and alcohol intake.–[3]95% confidence interval.–[4]Amount unknown.

TABLE III – RELATIVE RISK (RR) OF COLORECTAL CANCER MORTALITY ASSOCIATED WITH INDUSTRY/OCCUPATION, LUTHERAN BROTHERHOOD COHORT (1966–1986)

Industry/occupation[1]	Cohort (person-years	Colon (n = 120)			Colon and rectum (n = 145)		
		Number of deaths[2]	RR[3]	95% CI[4]	Number of deaths[2]	RR[3]	95% CI[4]
Occupation within industry							
Farm workers/agriculture	89,991	26	1.0	—	35	1.0	—
Crafts workers/service and trade	12,606	8	2.6	1.1–5.8	10	2.3	1.1–4.8
Crafts workers/mining and manufacturing	32,251	4	1.0	0.3–3.0	4	0.8	0.3–2.3
Semi-skilled/transportation and trade	12,046	10	1.7	0.8–3.7	13	1.6	0.8–3.1
Semi-skilled/mining and manufacturing	18,335	10	1.0	0.5–2.2	14	1.1	0.6–2.0
Professional/service and trade	81,708	39	1.7	1.0–3.0	43	1.4	0.9–2.3
Professional/mining and manufacturing	25,443	9	1.5	0.7–3.3	10	1.3	0.6–2.7

[1]Industry and occupation held for the longest period of time as of 1966.–[2]Subjects with missing information on industry or occupation were excluded.–[3]Adjusted for age, smoking, alcohol intake and physical activity.–[4]95% confidence interval.

ecologic correlation of meat/fat consumption with colorectal cancer mortality among various countries, associations seen in analytical studies, and the plausible biological mechanism that fat intake may increase bile acid excretion, thereby increasing the exposure of colonic mucosa to secondary bile acid, a potential tumor promoter. In addition, cooked meats have been shown to contain large amounts of heterocyclic amines, carcinogens produced by high-temperature cooking (Ames, 1983). In our study, only 35 food items were included in the 1966 food-frequency questionnaire and a few food items that contribute to dietary fat in the U.S. diet (such as liver, cheese, butter and processed meat) were not included. Therefore, we could not examine in detail the relative roles of red meat *vs.* saturated fat in colon cancer risk.

Sugar intake, especially sucrose, has been reported as an independent risk factor for colorectal cancer in a few studies (Bostick *et al*., 1994; La Vecchia *et al*., 1993). The epidemiologic evidence concerning a causal role of sugar is preliminary, though it has been reported that a diet rich in simple sugar may increase colonic cell proliferation, transit time and the fecal concentration of secondary bile acid, thereby increasing the risk of colon cancer (Kruis, 1991). We have no direct measurement on sugar or sucrose intake; however, we found no association with sugar added to coffee and consumption of sweet soup.

Contrary to most previous reports (Potter *et a*l., 1994), we did not find a protective effect of fruits and vegetables in this prospective study. This inconsistency may be explained in part by the significant positive correlation between meat and vegetable consumption ($r = 0.3$; $p < 0.0001$) in the Scandinavian diet since meat and vegetables usually are served together.

Large-scale prospective studies have reported a positive association of smoking with colorectal cancer and colon adenoma in both men and women (Giovannuci *et al.,* 1994*a,b*; Heineman *et al.,* 1994). In these studies, a 20–40% excess risk was observed for cancer of the colon, and it appears that the excess risk is mostly in long-term and heavy smokers. Furthermore, most colon adenoma studies have reported a positive association with cigarette smoking (Heineman *et al.,* 1994). Thus, the role of tobacco use in colorectal cancer etiology needs further evaluation. In our follow-up study, heavy smokers (30 cigarettes/day) had a 2-fold increased risk and long-term users (30 years) had a 20% excess risk, though the dose-response trend was not statistically significant.

The effect of alcohol consumption on colorectal cancer is not clear (IARC, 1988). Alcohol use has been related to colon cancer (Giovannucci *et al*., 1995), with a meta-analysis estimating that total intake of alcoholic beverages (2 drinks/day) may be related to

TABLE IV – RELATIVE RISK (RR) OF COLORECTAL CANCER BY QUARTILE INTAKE LEVELS OF SELECTED FOOD GROUPS, LUTHERAN BROTHERHOOD COHORT (1966–1986)

Food groups (quartile) (times/month)[1]	Cohort (person-years)	Colon (n = 120)			Colon and rectum (n = 145)		
		Number of deaths	RR[2]	95% CI[3]	Number of deaths	RR[2]	95% CI[3]
Red meat							
<15	50,613	19	1.0	—	24	1.0	—
15–19	32,114	15	1.2	0.6–2.5	16	1.2	0.6–2.2
20–29	83,655	37	1.4	0.8–2.5	45	1.5	0.9–2.5
30–59	97,293	36	1.2	0.7–2.3	46	1.4	0.8–2.5
≥60	23,407	13	1.8	0.8–4.4	14	1.9	0.9–4.3
		Linear trend $p = 0.3$			Linear trend $p = 0.1$		
Poultry							
Q1 (<0.5)	28,551	9	1.0	—	13	1.0	—
Q2 (0.5–1.4)	104,570	42	1.1	0.5–2.3	51	1.0	0.5–1.8
Q3 (1.5–4.0)	109,660	44	1.1	0.5–2.3	56	1.0	0.5–1.9
Q4 (>4.0)	44,298	25	1.6	0.7–3.6	25	1.1	0.5–2.2
		Linear trend $p = 0.2$			Linear trend $p = 0.7$		
Fish							
Q1 (<0.8)	62,477	21	1.0	—	24	1.0	—
Q2 (0.8–1.6)	89,156	34	1.0	0.5–1.7	44	1.1	0.7–1.9
Q3 (1.7–4.0)	77,518	30	1.0	0.6–1.8	37	1.2	0.7–2.0
Q4 (>4.0)	57,930	35	1.4	0.8–2.5	40	1.5	0.9–2.6
		Linear trend $p = 0.2$			Linear trend $p = 0.1$		
Eggs							
Q1 (<4.0)	66,759	25	1.0	—	33	1.0	—
Q2 (4.0–8.9)	90,148	39	1.2	0.7–2.0	46	1.1	0.7–1.7
Q3 (9.0–21.0)	80,963	34	1.3	0.8–2.3	39	1.2	0.7–1.9
Q4 (>21.0)	49,211	22	1.3	0.7–2.5	27	1.3	0.7–2.4
		Linear trend $p = 0.4$			Linear trend $p = 0.4$		
Dairy products							
Q1 (<26.0)	81,570	46	1.0	—	56	1.0	—
Q2 (26.0–50.0)	68,916	29	0.8	0.5–1.3	36	0.8	0.5–1.2
Q3 (51.0–85.0)	76,932	28	0.7	0.4–1.1	34	0.7	0.4–1.3
Q4 (>85.0)	59,662	17	0.6	0.3–1.3	19	0.6	0.3–1.2
		Linear trend $p = 0.1$			Linear trend $p = 0.1$		
Vegetables							
Q1 (<1.2)	69,947	28	1.0	—	37	1.0	—
Q2 (1.2–2.1)	71,215	26	1.1	0.6–1.9	35	1.1	0.7–1.8
Q3 (2.2–4.5)	73,780	33	1.4	0.8–2.4	37	1.2	0.8–2.4
Q4 (>4.5)	72,139	33	1.5	0.8–2.8	36	1.3	0.8–2.4
		Linear trend $p = 0.3$			Linear trend $p = 0.3$		
Cruciferous vegetables							
Q1 (<1.2)	78,565	26	1.0	—	34	1.0	—
Q2 (1.2–2.1)	70,840	25	1.0	0.6–1.7	30	0.9	0.6–1.6
Q3 (2.2–4.5)	70,025	28	1.0	0.6–1.8	34	0.9	0.6–1.5
Q4 (>4.5)	67,652	41	1.4	0.9–2.4	47	1.4	0.9–2.2
		Linear trend $p = 0.2$			Linear trend $p = 0.2$		
Fruits							
Q1 (<29.3)	71,975	24	1.0	—	28	1.0	—
Q2 (29.3–46.4)	73,721	25	1.0	0.6–1.9	33	1.2	0.7–2.1
Q3 (46.5–67.0)	71,052	35	1.6	0.9–2.8	43	1.7	1.0–2.8
Q4 (>67.0)	70,333	36	1.6	0.9–2.9	41	1.6	0.9–2.8
		Linear trend $p = 0.05$			Linear trend $p = 0.04$		
Bread							
Q1 (<88)	71,573	30	1.0	—	36	1.0	—
Q2 (88–138.7)	70,126	32	1.0	0.6–1.7	42	1.1	0.7–1.7
Q3 (138.8–176.3)	72,066	30	0.8	0.5–1.5	35	0.9	0.5–1.4
Q4 (>176.3)	73,316	28	0.8	0.4–1.5	32	0.8	0.5–1.4
		Linear trend $p = 0.4$			Linear trend $p = 0.3$		

[1]Monthly consumption in 1966. Food items included in each food group are as follows: red meat: beef, bacon, fresh pork and smoked ham; poultry: chicken; fish: fresh fish, salted fish and fish balls; dairy products: milk and ice cream; vegetables: potatoes, green salad, tomatoes, carrots, peas, corn, beans, vegetable soup, cabbage, cauliflower, pea soup and rutabaga; cruciferous vegetables: cabbage, cauliflower and rutabaga; fruits: fruit juice, canned fruit, apples, bananas, oranges, grapes and fruit soup; bread: bread, packaged cereal, cooked cereal, pancakes and flat bread.–[2]Adjusted for age, smoking, alcohol intake and total calories.–[3]95% confidence interval.

a 10% excess risk and showing that consumption of beer is related to a 26% excess (Longnecker, 1990). In our study, we found significantly elevated risks among heavy beer users and ever users but weak and non-significant risk among users of total alcohol and liquor. It is not clear whether any elevated risk may be related to alcohol *per se* or to constituents, such as nitrosamines, in beer (Preussmann, 1984).

Consistent with earlier studies, we found excess colon cancer risk among white-collar workers and craftsman who worked within the service and trade industries. The observed elevated risks may, in part, reflect the relatively low physical activity required by these occupations. However, we did not have detailed occupational and industrial histories to evaluate colon cancer risk associated with specific exposures.

Several limitations of our study should be noted. Since information on risk factors was collected once only, in 1966, dietary patterns and smoking and drinking habits among cohort members could have changed with time and mis-classification of these exposures is thus likely. However, such mis-classification is likely to be non-differential and would tend to lead to an under-estimation of a true effect. In addition, about 23% of the cohort members were lost to follow-up due to lapsed or matured policies. There were no significant differences, however, in tobacco, alcohol or dietary intake between active members and those lost to follow-up at 20 years. Thus, selection bias introduced by attrition in the study is likely to be minimal. Generalizability of the study may be limited because the LBS cohort is a self-selected group, with more farmers, rural residents and individuals of Scandinavian descent than in the United States as a whole (Snowden, 1981). In addition, because mortality is used in the study as the end point, the results may not generalize to the less invasive and aggressive types of colorectal cancer. The statistical power of the study is limited due to the relatively small number of colorectal cancer deaths. Since there were only 25 rectal cancer deaths, we were unable to conduct a separate analysis for this subsite.

In summary, our cohort study provides further evidence that cigarette smoking, beer drinking, a high consumption of red meat and sedentary occupations may be associated with an increased risk of colon cancer mortality. Further studies are needed to clarify the role of these factors in the etiology of colon cancer.

ACKNOWLEDGEMENTS

We thank Ms. N. Odaka and Mr. W. Hufford at Westat for excellent computer support.

REFERENCES

Ames, B.N., Dietary carcinogens and anticarcinogens: oxygen radicals and degenerative diseases. *Science,* **221**, 1256–1264 (1983).

Armstrong, B. and Doll, R., Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. *Int. J. Cancer*, **15**, 617–631 (1975).

Bostick, R.M., Potter, J.D., Kushi, L.H., Sellers, T.A., Steinmetz, K.A., McKenzie, D.R., Gapstur, S.M. and Folsom, A.R., Sugar, meat, and fat intake, and non-dietary risk factors for colon cancer incidence in Iowa women (United States). *Cancer Causes Control,* **5**, 38–52 (1994).

Bostick, R.M., Potter, J.D., Sellers, T.A., McKenzie, D.R., Kushi, L.H. and Folsom, A.R., Relation of calcium, vitamin D, and dairy food intake to incidence of colon cancer among older women. *Amer. J. Epidemiol*., **137**, 1302–1317 (1993).

Breslow, N.E. and Day, N.E., *Statistical Methods in Cancer Research*, Vol. **2**, pp. 120–176, International Agency for Research on Cancer, IARC Scientific Publication **82**, Lyon (1987).

Chow, W., Malker, H.S.R., Hsing, A.W., McLaughlin, J.K., Stone, B.J., Ericsson, J.L.E. and Blot W.J., Occupational risks for colon cancer in Sweden. *J. Occup. Med.,* **36**, 647–651 (1994).

Chow, W.H. and Devesa, S.S., Death certificate reporting of colon and rectal cancers. *J. Amer. med. Ass.*, **267**, 3028 (1992).

Colditz, G.A., Cannuscio, C.C. and Frazier, A.L., Physical activity and reduced risk of colon cancer: implications for prevention. *Cancer Causes Control*, **8,** 649–667 (1997).

Giovannucci, E., Colditz, G.A., Stampfer, M.J., Hunter, D., Rosner, B.A., Willett, W.C. and Speizer, F.E., A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U.S. women. *J. nat. Cancer Inst*., **86**, 192–199 (1994*a*).

Giovannucci, E. and Goldin, B., The role of fat, fatty acids, and toal energy intake in the etiology of human colon cancer. *Amer. J. clin. Nutr.*, **66** (Suppl. 6),1564S–1671A (1997).

Giovannucci, E. and Martinez, M.E., Tobacco, colorectal cancer, and adenomas: a review of the evidence. *J. nat. Cancer Inst.* **88,** 1717–1730 (1996).

Giovannucci, E., Rimm, E.B., Ascherio, A., Stampfer, M.J., Colditz, G.A. and Willett, W.C., Alcohol, low-methionine–low-folate diets, and risk of colon cancer in men. *J. nat. Cancer Inst*., **87**, 265–273 (1995).

Giovannucci, E., Rimm, E.B., Stampfer, M.J., Colditz, G.A., Ascherio, A., Kearney, J. and Willett, W.C., A prospective study of cigarette smoking and risk of colorectal adenoma and colorectal cancer in U.S. men. *J. Nat. Cancer Inst*., **86**, 183–191 (1994*b*).

Giovannucci, E., Rimm, E.B., Stampfer, M.J., Colditz, G.A., Ascherio, A. and Willett, W.C., Intake of fat, meat, and fiber in relation to risk of colon cancer in men. *Cancer Res*., **54**, 2390–2397 (1994*c*).

Glynn, S.A., Albanes, D., Pietinen, P., Brown, C.C., Rautalahi, M., Tangrea, J.A., Taylor, P.R. and Virtamo, J., Alcohol consumption and risk of colorectal cancer in a cohort of Finnish men. *Cancer Causes Control*, **7**, 214–223 (1996).

Heilbrun, L.K., Nomura, A., Hankin, J.H. and Stemmermann, G.N., Diet and colorectal cancer with special reference to fiber intake. *Int. J. Cancer*, **44**, 1–6 (1989).

Heineman, E.F., Zahm, S.H., McLaughlin, J.K. and Vaught, J., Increased risk of colorectal cancer among smokers: results of a 26-year follow-up of U.S. veterans. *Int. J. Cancer,* **59**, 728–738 (1994).

Hsing, A.W., McLaughlin, J.K., Schuman, L.M., Bjelke, E., Gridley, G., Wacholder, S., Co Chien, H.T. and Blot, W.J., Diet, tobacco use and fatal prostate cancer: results from the Lutheran Brotherhood cohort study. *Cancer Res*., **50**, 6836–6840 (1990).

International Agency for Research on Cancer, *Alcohol Drinking*, IARC Monograph **44,** IARC, Lyon (1988).

International Agency for Research on Cancer , *Tobacco Smoking*, IARC Monograph **38,** IARC, Lyon(1986).

Kruis, W., Forstmaier, G., Sheurlen, C. and Stellaard, F., Effect of diets low and high in refined sugars on gut transit, bile acid metabolism, and bacterial fermentation. *Gut*, **32**, 367–371 (1991).

Kune, G.A. and Vitetta, L., Alcohol consumption and the etiology of colorectal cancer: a review of the scientific evidence from 1957 to 1991. *Nutr. Cancer*, **18**, 97–111 (1992).

La Vecchia, C., Franceschi, S., Dolara, P., Biddi, E. and Barbone, F., Refined sugar intake and the risk of colorectal cancer in humans. *Int. J. Cancer*, **55,** 386–389 (1993).

Longnecker, M.P., Orza, M.J., Adams, M.E., Vioque, J. and Chalmers, T.C., A meta-analysis of alcoholic beverage consumption in relation to risk of colorectal cancer. *Cancer Causes Control*, **1**, 59–68 (1990).

Martinez, M.E., McPherson, R.S., Annegers, J.F. and Levin, B., Cigarette smoking and alcohol consumption as risk factors for colorectal adenomatous polyps. *J. nat. Cancer Inst*., **87**, 274–279 (1995).

Parker, S.L., Tong, T., Bolden, S., Wingo, P.A., Cancer statistics, 1997. *CA Cancer J. Clin*., **47,** 5–27 (1997).

Potter, J.D., Slattery, M., Bostick, R. and Gapstur, S.M., Colon cancer: a review of the epidemiology. *Epidemiol. Rev*., **15**, 499–545 (1994).

Preston, D.I., Kopecky, K.J. and Kato, H., Analysis of mortality and disease incidence among atomic bomb survivors. *In* W.J. Blot, T. Hirayama and D.G. Heol (eds.), *Statistical methods in cancer epidemiology,* pp. 49–62. Radiation Effects Research Foundation, Hiroshima (1985).

Preussmann, R., Occurrence and exposure to *N*-nitroso compounds and precursors. *In* I.K. O'Neill, R.C. von Borstel and C.T. Miller (eds.), N-*nitroso compounds: occurrence, biological effects and relevance to human cancer,* pp. 3–5, IARC Scientific Publication **57,** Lyon (1984).

Schottenfeld, D., Winawer, S.J., Cancers of the large intestine. *In* D. Scgottenfeld and J.F. Fraumeni, Jr. (eds.), *Cancer epidemiology and prevention* (2nd ed.), Oxford University Press, New York (1996).

Snowden, D.A., Alcohol use and mortality from cancer and heart disease among members of the Lutheran Brotherhood cohort. Ph.D. Dissertation, University of Minnesota (1981).

Steinmetz, K.A., Kushi, L.H., Bostick, R.M., Folsom, A.R. and Potter, J.D., Vegetables, fruit, and colon cancer in the Iowa Women's Health Study. *Amer. J. Epidemiol.*, **139**, 1–15 (1994).

Thomas, H.J., Familial colorectal cancer. *Brit. med. J.*, **307**, 277–278 (1993).

Thun, M.J., Calle, E.E., Namboodiri, M.M., Flanders, W.D., Coates, R.J., Byers, T., Boffetta, P., Garfinkel, L. and Heath, C.W., Jr., Risk factors for fatal colon cancer in a large prospective study. *J. nat. Cancer Inst*., **84**, 1491–1500 (1992).

Willett, W.C., Stampfer, M.J., Colditz, G.A., Rosner, B.A. and Speizer, F.E., Relation of meat, fat, and fiber intake to the risk of colon cancer in a prospective study among women. *N. Engl. J. Med*., **323**, 1664–1672 (1990).